

Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 20 claims. These were cancelled and replaced with claims 21-27. All of these have now been cancelled and new claims 28-40 have been added.

II. The Amendments

The amendments made herein are all supported by the specification and claims in the application as filed. The main element that appears not to have been in claims previously is the requirement that samples be obtained from individuals not previously diagnosed as having prostate cancer (paragraph a of claim 28). Support for this amendment may be found on page 10 of the substitute specification filed on May 20, 2002, paragraphs 0047 and 0048.¹

The present amendments do not add new matter to the application and their entry is therefore respectfully requested.

The Rejections

I. Rejection of Claims Under 35 USC § 112

On pages 2-3 of the Office Action, the Examiner rejects claims 21-26 based upon the allegation that the phrase "reporting an increased risk for prostate cancer in the healthy individual" is indefinite.

In response, Applicants have eliminated the phrase that the Examiner has cited. It is therefore respectfully submitted that this rejection has been obviated.

¹ These same paragraphs appear on page 4 of the published application as paragraphs 0050 and 0051.

II. Rejection of Claims Under 35 USC § 102

On pages 3-4 of the Office Action, claims 21-26 are rejected under 35 USC § 102(b) as anticipated by either Juul-A (Juul, *et al.*, *J. Clin. Endocrinol. Metab.* 78:744-752 (1994)) or Juul-B (Juul, *et al.*, *Clin. Endocrinol.* 41:85-93 (1994)).

Juul-B reports that the IGF-1/IGFBP-3 ratio decreases with age in normal people but that this ratio remains higher in agromegaly patients having high levels of growth hormone (see abstract). The main conclusion of the paper appears to be that both IGF-1 and IGFBP-3 levels are affected by growth hormone. The reference does not suggest using the IGF-1/IGFBP-3 ratio as a method of diagnosing prostate cancer. It also does not suggest distinguishing the people assayed for IGF-1/IGFBP levels and compared with a normal group based upon whether the individuals have had prostate cancer or not. Thus, a manipulative step required in paragraph a) of claim 28 (the selection of samples based on cancer status) is not present in Juul-B and, as a result, the reference is not an anticipation.

Juul-A describes changes in IGF-1 levels that occur during childhood and the problems of using these levels to distinguish between children with retarded pubertal development and those with a growth hormone deficiency (see abstract). As with Juul-B, this reference fails to suggest selecting samples based upon the cancer status of the individuals that they are obtained from. It also fails to suggest a procedure in which IGFBP-3 levels are determined. It is therefore submitted that Juul-A does not anticipate the claims as amended herein.

Although Applicants believe that the factors discussed above are sufficient to overcome the rejection of all claims as anticipated by Juul-A or Juul-B, it should be noted that there is an additional factor, the measurement of PSA levels that applies with respect to claims 38-47.

II. Rejection of Claims Under 35 USC § 103

On pages 4-6 of the Office Action, claims 21-26 are rejected as obvious in light of Mantzoros, *et al.* (*British J. Cancer* 76:1115-1118 (1997)). The Examiner argues that Mantzoros teaches that IGF-1 levels are elevated in patients with prostate cancer.

Applicants respectfully traverse this rejection for the claims as amended herein.

Applicants do not dispute the allegation that Mantzoros reported an increased level of IGF-1 in patients with prostate cancer. However, Mantzoros does not suggest measuring IGBP-3 along with IGF-1, comparing the ratio of the two with a reference range of ratios and using this as a predictor of prostate cancer risk. In this regard, it should be noted that Applicants found that a comparison based on a multivariate analysis produced substantially better results than the use of IGF-1 levels alone (see *e.g.*, paragraph 0054 on pages 13-14 of the substitute specification filed on May 20, 2002).² Based on these considerations, Applicants submit that one could not arrive at the presently claimed methods based upon the teachings of Montzoros. It is therefore respectfully requested that the rejection of claims on obviousness grounds be withdrawn.

Conclusion

In light of the discussion above, Applicants respectfully submit that all of the Examiner's rejections have been overcome. It is therefore requested that these rejections be withdrawn and that the claims now pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (240)683-6165.

Respectfully submitted,

LAW OFFICE OF MICHAEL A. SANZO

By: Michael A. Sanzo

Michael A. Sanzo

Reg. No. 36,912

Attorney for Applicants

Date: October 10, 2007
15400 Calhoun Drive, Suite 125
Rockville, Md. 20855
(240)683-6165

² The same paragraph appears in the published application on page 5 and is numbered as paragraph 57.